REMARKS

Alleged Lack of Enablement

Claims 34-36, 38-41, 43-45, and 47-3, all claims pending in this patent application, stand rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement with respect to their recitation *in vivo* extracellular administration. Although the Examiner acknowledges that those skilled in the art would be able to produce a biological response in living cells through *in vitro* extracellular administration of the recited compounds, the Examiner contends those skilled in the art would not be able to produce such a response through *in vivo* extracellular administration. Applicants respectfully request reconsideration and withdrawal of the rejection because there is no evidence of record indicating that those skilled in the art would not be able to achieve at least some measurable biological response through practice of the claimed methods.

When rejecting a claim under the enablement requirement of 35 U.S.C. § 112, first paragraph, the Patent Office bears the "initial burden of setting forth a reasonable explanation as to why [it] believes that the scope of protection provided by [the] claim is not adequately enabled by the description of the invention provided in the specification." *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). To object to a specification on the grounds that the disclosure is not enabling with respect to the scope of a claim sought to be patented, the Examiner must provide evidence or technical reasoning substantiating those doubts. *In re Marzocchi*, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971); M.P.E.P. § 2164.04. Without a reason to doubt the truth of the statements made in the patent application regarding practice of the claimed subject matter, the application must be considered enabling. *In re Wright*, 27 U.S.P.Q.2d at 1513; *In re Marzocchi*, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971).

Here, however, the Examiner fails to identify objective evidence indicating that the claimed methods would not produce at least some measurable biological response. The Examiner cites a number of publications demonstrating that issues such as cellular uptake of the recited compounds "ha[ve] to be considered" and "should be investigated" (Office Action at page 6), but none of these publications indicate that the recited compounds will not perform in the manner contemplated by Applicants' claims. Similarly, although the Office

Action cites publications indicating that certain issues relating to the recited compounds "must be addressed before reaching [the] ultimate goal" of using them as "an antisense or antigene drug for sequence-specific modulation of gene expression" (*id.* at page 7), none of these publications indicates that the compounds do not produce at least some measurable level of the claimed biological response. As will be recognized, the claims do not require that the recited compounds satisfy the rigorous efficacy standards that typically are imposed (by, for example, the FDA) upon commercialized drugs; rather, all that the claims require is that the recited compounds produce some biological response.

Further evidence supporting enablement of the instant claims is provided by U.S. 6,472,209, in the name of Richelson, *et al.* ("the Richelson patent), which issued nearly eight years ago on an application that was filed after the effective filing date of the instant patent application. Claim 1 of the Richelson patent, for example, is directed to at least substantially the same subject matter as that recited in Applicants' claims:

> 1. A method of treating living cells, said method comprising extracellularly administering to said cells a polyamide nucleic acid oligomer containing neutral amide backbone linkages which is complementary to a target nucleic acid, under conditions wherein a biological response associated with said target in a sequence specific manner, said administration being in vivo.

The Richelson patent is also relevant to enablement of Applicants' claimed methods in view of the Federal Circuit's decision in *Agilent Technologies, Inc., v. Affymetrix, Inc.*, 567 F.3d. 1366 (Fed Cir. 2009). In *Agilent*, the Federal Circuit considered the issue of how claims should be interpreted when they have been copied from a patent or patent application with which interference is sought, specifically, "whether the copying party's specification ... adequately support[s] the subject matter claimed by the other party" (citing *In re Spina*, 979 F.2d 854 (Fed. Cir. 1992). Distinguishing its prior decision in *Rowe v. Dror*, 112 F.3d 473 (Fed. Cir. 1997), the Court in *Agilent* held that where the PTO must assess whether parties have a right to claim the same subject matter "the claim construction analysis properly occurs in the context of the specification from which the claims were copied" *Agilent*, 567 F.3d at 1375.

The Federal Circuit's decision in *Agilent* is relevant here because the pending claims include language copied from the Richelson patent claims, and also because there is disclosure in the Richelson patent which bears on enablement of the claimed subject matter. As Applicants stated in the Preliminary Amendment filed in the instant patent application, certain of the currently pending claims have been copied from the Richelson patent, and others are at least directed to substantially the same subject matter as claims which issued in that patent. (Preliminary Amendment dated October 22, 2003, at page 9).

Among the claim language copied from the Richelson patent claims is the phrase "under conditions wherein said oligomer engenders a biological response associated with said target in a sequence specific manner." (*see, e.g.,* Richelson patent claim 1 and pending claims 34, 41, 49, and 58). There is considerable disclosure in the Richelson patent that relates to this phrase and supports enablement of the instant claims. At column 7, lines 4-10, for example, the Richelson patent states as follows:

> The desired sequence specific biological response can be any alteration of a particular activity or can be a specific level of alternation of a particular activity. For example, one desired sequence specific biological response could be any reduction in polypeptide expression, whereas another could be the complete knock-out of polypeptide expression.

The patent provides further disclosure regarding "biological response" at column 3, lines 26 – 30:

> The biological response engendered by the extracellular administration of PNA oligomers can be a modification, for example a reduction of polypeptide expression. Biological responses also can be characterized by a physiological change in an animal.

Still further disclosure is provided in the Richelson patent at column 5, lines 53-65:

> Thus, a sequence specific biological response is any response of a living cell that is attributed to the actual sequence of a PNA oligomer, such as the alternation of protein X expression as stated above. In addition to analyzing polypeptide expression, sequence specific biological responses can be determined by analyzing any biological activity including, without limitation, cellular activities such as signaling, adherence, movement, proliferation, differentiation, and apoptosis as well as physiological activities such as development, growth, reproduction, immunity, pain, anti-nociception, perception, depression, and memory.

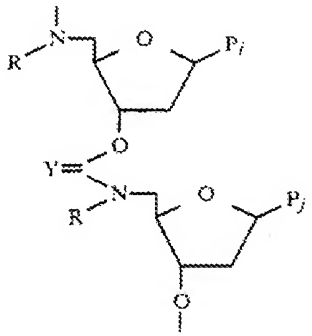
This disclosure supports Applicants' position that those skilled in the art would have been able to practice the claimed methods to at least some measurable extent. This disclosure, together with the absence of contrary evidence, also warrants withdrawal of the rejection under Section 112, first paragraph.

Alleged Anticipation

Claims 34-36, 41, 48-51, 58, 59, and 65-68 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 5,142,047 ("the Summerton patent"). This rejection is improper because the Summerton patent is alleged to be relevant for its disclosure of compounds that have a different structure than those recited in the instant claims.

For a reference to be anticipatory, it must describe "all elements of [the] claimed invention arranged as in that claim." *Carella v. Starlight Archery*, 804 F.2d 135, 138 (Fed. Cir. 1986); *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1267 (Fed. Cir. 1991). Importantly, for a rejection to be proper under 35 U.S.C. § 102, the reference must "clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without *any* need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference." *In re Arkley*, 172 U.S.P.Q. 524, 526 (C.C.P.A. 1972) (emphasis in original).

The Summerton patent does not satisfy these requirements. The Examiner asserts that the linkages recited in the instant claims correspond to the linkage used in the following compound in the Summerton patent (Office Action at pages 11-12).



However, this linkage (*i.e.,* **-O-**C(=O)-NR- when Y is oxygen) is a carbamate linkage (a derivative of a carbonic acid), whereas the rejected claims recite an amide linkage (*i.e.*, **-C-**C(=O)-NR-) (a derivative of a carboxylic acid). Thus, there is no anticipation.

When Applicants' brought this distinction to the Examiner's attention, the Examiner asserted that if one ignores the non-carbonyl oxygen atom in the –O-CO-NR- linkage, "the reference is viewed as containing the neutral amide linkage (underlined) as instantly claimed." (*id.*). Such an interpretation, however, is not consistent with the understanding of a person skilled in the art. Those skilled in the art regard the "ignored" oxygen atom as integral to the structure of a carbamate group. Moreover, those skilled in the art would not simply ignore a functional atom in analyzing the linkage for various reasons, not the at least being the profound difference in electronic properties an oxygen atom verses a nitrogen atom verses a carbon atom have when position adjacent to the CO-NR- group. These differences in electronic properties are of fundamental importance to the nature of the group. A person skilled the art would not ignore the disputed oxygen atom (and view the remaining –CO-NR- portion of –O-CO-NR- as an amide) any more than they would also ignore the NR group (and view the remaining –O-CO- portion of –O-CO-NR- as an ester).

Additionally, in ignoring the oxygen atom of the Summerton structure the Examiner gives no indication of the fate of the pair of electrons that bond between the oxygen atom and the carbon atom of the carbonyl radical. If the pair of electrons are removed with the oxygen atom (after all oxygen is more electro negative that carbon) a carbocation results. Of course a carbocation has a net positive charge. A net positive charge is not neutral, as required by the claims at issue. If the pair of electrons is left with the carbon atom of the carbonyl group a carbanion results. Such carbanion has a net negative charge. A net negative charge is also not neutral as is required by the claims at issue.

The Summerton patent also refutes the Examiner's position that the oxygen atom can be ignored. The structure reproduced in the outstanding Office Action is found in column 5 of the Summerton patent, and is designated as structure "B-B". In column 6, lines 49-51, the Summerton patent refers to B-B as a carbamate-linked structure, not an amide-linked structure.

In the outstanding Office Action, the Examiner alleges that the carbamate (*i.e.*, -O-C(=O)-NR-) linkage disclosed in the Summerton patent is anticipatory because: (1) Applicants' claims refer to compounds "containing neutral amide backbone linkages" and (2) the carbamate backbone linkage is one "viewed as containing amide" (*id.*). Applicants note, however, that the pending claims are not directed to compounds that (as in the Summerton patent) contain backbone linkages that, in turn, "contain amide." Rather, the claims are directed to compounds that "contain[] neutral amide backbone linkages."

Because the structure that the Summerton patent discloses is different from that recited in the instant claims, the rejection for alleged anticipation is improper and should be withdrawn.

Conclusion

Applicants believe the foregoing constitutes a complete response to the Office Action and submit that all pending claims are in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,

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